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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/524,653	02/17/2005	Zhan-qi Niu	UNI-05-1016	8338

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EXAMINER	
HENRY, MICHAEL C	
ART UNIT	**PAPER NUMBER**
1623	

MAIL DATE	DELIVERY MODE
09/27/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/524,653	NIU ET AL.	
	Examiner	Art Unit	
	Michael C. Henry	1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-16 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1-16 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date 02/17/05 & 10/13/06.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-16 are pending in application

Information Disclosure Statement

The information disclosure statement filed complies with the provisions of 37 CFR 1.97, 1.98 and MPEP § 609. It has been placed in the application file and the information referred to therein has been considered as to the merits.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-5, 12-14, 16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Xu et al. (Yao Xue Xue Bao = Acta Pharmaceuticals Sinica, (2001 May) vol. 36, No. 5, pages 329-333) in view of Habon et al. (Pharmazie (1984), 39 (12), pages 830-4).

In claim 1, applicant claims an inclusion complex of butylphthalide with cyclodextrin or cyclodextrin derivatives, comprising butylphthalide and cyclodextrin or cyclodextrin derivative, wherein the molar ratio of butylphthalide to cyclodextrin or cyclodextrin derivatives is 1:1-10. Claims 2-5 are drawn to said inclusion complex involving the use of specific types of cyclodextrins. Claims 12-14 are drawn to a pharmaceutical composition comprising said complex and specific forms of said composition.

Xu et al. disclose butylphthalide which has antithrombotic activity and antiplatelet activity when administered to rats (see abstract).

The difference between applicant's claimed compound or composition and the compound or composition of Xu et al. is that applicant's compound is complexed with cyclodextrin.

Habon et al. disclose that complexation of drugs with cyclodextrin enhances the bioavailability of drugs in vivo (see abstract). Furthermore, Habon et al. disclose that the ennhanced the bioavailability of drugs upon complexation are due factors such as enhanced dissolution rates and higher solubility (see abstract). In addition, Habon et al. disclose that the enhanced bioavailability is controlled or depends on factors such as solubilities, stability constants and the molar ratio of drug to cyclodextrin. Habon et al. disclose that the compounds can be administered in oral dosage forms (see abstract).

It would have been obvious to one having ordinary skill in the art at the time the claimed invention was made in view of Xu etal. and Habon et al. to have prepared a complex of butylphthalide with cyclodextrin or a derivative in order to the enhance the bioavailability of the drug due to complexation by administering said complex to a subject and consequently to improve the treatment of thrombosis.

One having ordinary skill in the art would have been motivated in view of Xu etal. and Habon et al. to have prepared a complex of butylphthalide with cyclodextrin or a derivative in order to enhance the bioavailability of the drug due to complexation by administering said complex to a subject and consequently to improve the treatment of thrombosis, based on factors such as the severity of the thrombosis and the type of subject treated. It should be noted that the use of specific ratios of drug to cyclodextrins also depends on factors such as the severity of the thrombosis and the type of subject treated. It should be noted that the use of specific forms or formulations of said drugs

such as butylphthalide is well-known in the art and is well within the purview of a skilled artisan.

In claim 16, applicant claims a method of treating thrombosis comprising administering a therapeutically effective amount of the inclusion complex according to claim 1 to a patient.

Xu et al. disclose a method of treating thrombosis by administering butylphthalide having antithrombotic activity and antiplatelet activity to rats (see abstract).

The difference between applicant's claimed method and the method of Xu et al. is that applicant's compound is complexed with cyclodextrin.

Habon et al. disclose that complexation of drugs with cyclodextrin enhances the bioavailability of drugs in vivo (see abstract). Furthermore, Habon et al. disclose that the ennhanced bioavailability of drugs upon complexation are due factors such as enhanced dissolution rates and higher solubility (see abstract). In addition, Habon et al. disclose that the enhanced bioavailability is controlled or depends on factors such as solubilities, stability constants and the molar ratio of drug to cyclodextrin. Habon et al. disclose that the compounds can be administered in oral dosage forms (see abstract).

It would have been obvious to one having ordinary skill in the art at the time the claimed invention was made in view of Xu et al. and Habon et al. to use the method of Xu et al. to treat thrombosis in a subject by administering a complex of butylphthalide with cyclodextrin or a derivative to said subject in order to enhance the bioavailability of the drug due to complexation and consequently to improve the treatment of thrombosis.

One having ordinary skill in the art would have been motivated in view of Xu et al. and Habon et al. to use the method of Xu et al. to treat thrombosis in a subject by

administering a complex of butylphthalide with cyclodextrin or a derivative to said subject in order to enhance the bioavailability of the drug due to complexation and consequently to improve the treatment of thrombosis, based on factors such as the severity of the thrombosis and the type of subject treated. It should be noted that the use of specific ratios of drug to cyclodextrins also depends on factors such as the severity of the thrombosis and the type of subject treated.

Claims 6-11 are rejected under 35 U.S.C. 103(a) as being unpatentable over Habon et al. (Pharmazie (1984), 39 (12), pages 830-4) in view of Xu et al. (Yao Xue Xue Bao = Acta Pharmaceuticals Sinica, (2001 May) vol. 36, No. 5, pages 329-333).

In claim 6, applicant claims a process for preparing the inclusion complex of butylphthalide with cyclodextrin or cyclodextrin derivatives, comprising the steps of adding cyclodextrin or cyclodextrin derivatives into a suitable solvent vehicle to obtain a solution with a concentration of 5-60%, adding butylphthalide into the solution, stirring to obtain a liquid inclusion complex of butylphthalide with cyclodextrin or cyclodextrin derivatives. Claims 7-8 are drawn to said process further involving steps of drying, precipitation and filtering to produce specific forms of said complex, and the use of specific solvents. Claims 9-10 are drawn to a process of preparing said inclusion complex with cyclodextrin or cyclodextrin derivatives comprising specific steps involving drying, precipitation and filtering to produce specific forms of said complex, and the use of specific solvents.

Habon et al. disclose a method of complexation of drugs with cyclodextrin to enhances the bioavailability of said drugs in vivo (see abstract). Furthermore, Habon et al. disclose that the enhanced the bioavailability of drugs upon complexation are due

factors such as enhanced dissolution rates and higher solubility (see abstract). In addition, Habon et al. disclose that the enhanced bioavailability is controlled or depends on factors such as solubilities, stability constants and the molar ratio of drug to cyclodextrin. Habon et al. disclose that the compounds can be administered in oral dosage forms (see abstract).

The difference between applicant's claimed method and the method of Habon et al. is the type of drug used.

Xu et al. disclose that butylphthalide has antithrombotic activity and antiplatelet activity when administered to rats (see abstract).

It would have been obvious to one having ordinary skill in the art at the time the claimed invention was made in view of Habon et al. and Xu etal. to use the method of Habon et al. to prepare a complex of butylphthalide with cyclodextrin or a derivative in order to ennhance the bioavailability of drug due to complexation by administering said complex to a subject and consequently to improve the treatment of thrombosis.

One having ordinary skill in the art would have been motivated in view of Habon et al. and Xu etal. to use the method of Habon et al. to prepare a complex of butylphthalide with cyclodextrin or a derivative in order enhance the bioavailability of drug due to complexation by administering said complex to a subject and consequently to improve the treatment of thrombosis, based on factors such as the severity of the thrombosis and the type of subject treated. It should be noted that the use of specific ratios of drug to cyclodextrins also depends on factors such as the severity of the thrombosis and the type of subject treated. It should be noted that the use of specific forms or formulations of said drugs such as butylphthalide is well-known in the art and is

well within the purview of a skilled artisan. Also, the use of common solvents and conventional techniques such as drying, precipitation and filtration in order to purify or produce specific forms a compound such as butylphthalide is common in the well-known in the art and is well within the purview of a skilled artisan.

Claim 15 is rejected under 35 U.S.C. 103(a) as being unpatentable over Xu et al. (Yaoxue Xuebao (1999), 34(3), 172-175) in view of Habon et al. (Pharmazie (1984), 39 (12), pages 830-4).

In claim 15, applicant claims a method of treating ischemia-induced disease comprising administering a therapeutically effective amount of the inclusion complex according to claim 1 to a patient.

Xu et al. disclose a method of treating cerebral ischemia by administering butylphthalide to rats (see abstract).

The difference between applicant's claimed method and the method of Xu et al. is that applicant's compound is complexed with cyclodextrin.

Habon et al. disclose that complexation of drugs with cyclodextrin enhances the bioavailability of drugs in vivo (see abstract). Furthermore, Habon et al. disclose that the ennhanced bioavailability of drugs upon complexation are due factors such as enhanced dissolution rates and higher solubility (see abstract). In addition, Habon et al. disclose that the enhanced bioavailability is controlled or depends on factos such as solubilities, stability constants and the molar ratio of drug to cyclodextrin. Habon et al. disclose that the compounds can be administered in oral dosage forms (see abstract).

It would have been obvious to one having ordinary skill in the art at the time the claimed invention was made in view of Xu et al. and Habon et al. to use the method of

Xu et al. to treat ischemia such as ischemia-induced disease in a subject by administering a complex of butylphthalide with cyclodextrin or a derivative to said subject in order to enhance the bioavailability of the drug due to complexation and consequently to improve the treatment of thrombosis.

One having ordinary skill in the art would have been motivated in view of Xu et al. and Habon et al. to use the method of Xu et al. to treat ischemia such as ischemia-induced disease in a subject by administering a complex of butylphthalide with cyclodextrin or a derivative to said subject in order to ennhance the bioavailability of the drug due to complexation and consequently to improve the treatment of thrombosis, based on factors such as the severity of the thrombosis and the type of subject treated. It should be noted that the use of specific ratios of drug to cyclodextrins also depends on factors such as the severity of the thrombosis and the type of subject treated.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michael C. Henry whose telephone number is 571-272-0652. The examiner can normally be reached on 8.30am-5pm; Mon-Fri. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shaojia A. Jiang can be reached on 571-272-0627. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For

more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Michael C. Henry

9/24/07

Shaojia Anna Jiang, Ph.D.
Supervisory Patent Examiner
Art Unit 1623

September 22, 2007.